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## Office-Based Research: The Antidote to Learned Helplessness

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*Canadian Family Physician* is very pleased to be able to publish the modified text of that presentation for a wider audience.

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**A**NTIDOTES ARE usually prescribed for poisons, and I use the term deliberately because I am concerned about a poisonous state of affairs: a state of learned helplessness.

The easiest way to illustrate this concept is to recreate in one's imagination Martin Seligman's original experiments of the late 1960s.<sup>1</sup> Imagine a dog in a box with a shoulder-high barrier. The metal floor of the box is electrified. When a button is pressed, a mild series of shocks is delivered to the dog through the floor. The dog will run about until it stumbles over the barrier, thus escaping the shocks. On the next trial, the dog, running frantically, will cross the barrier sooner. Within a few episodes, the dog will become very adept at making a quick escape.

Picture a second dog that has been preconditioned by being kept in a har-

ness. Under that condition it could not escape the shocks no matter what it did. When this second dog is taken out of its harness and left unrestrained in the box with the shoulder-high barrier, its reaction to the shock is strikingly different from that of the first dog. Initially, it will run about as the other dog did, but only for 30 seconds. Then it will lie down and whine quietly. In essence, it gives up and passively accepts the shocks. It will repeat this behaviour on subsequent trials. The dog has learned to be helpless in face of the shocks.

This experiment demonstrates all the requirements for learned helplessness:

- preconditioning;
- perception that events are beyond the subject's control;
- adoption of that perception even if it is incorrect; and
- passive acceptance of the status quo.

Similar experimental work with humans has been directed towards investigating learned dependence, a more moderate degree of helplessness. In one experiment, Langer was able to show that an employee's performance can be affected just by labelling him "an assistant" in contrast to describing him as "the boss".<sup>2</sup> The experiment initially involved two groups of high school seniors set to completing word tasks. The researcher told one group that they were "assistants". He told the second group that they were solely responsible for completing the work. The "assistants" completed significantly fewer tasks; the "independents" showed no corresponding drop in performance. Thus something as simple as an "inferior" label can affect per-

formance through self-induced dependence.

The effect of learned dependence can be all the more devastating if it is supported by others. The classic example of this phenomenon is the dependence developed by the institutionalized elderly. The caring, concerned, nursing-home staff all too often foster dependence in the elderly residents.<sup>3</sup> They do so with the best of intentions. They help the elderly residents to get dressed and to bathe. As a result of this well-intentioned help, the elderly lose opportunities to practise necessary skills. More important, the message is given that they are not capable of self-care. Thus the residents are taught to be dependent.

How quickly this can come about was demonstrated in a study done by Avorn and Langer in 1983.<sup>4</sup> The research involved two groups of elderly residents in a nursing home. Both groups were set to work solving puzzles. One group was randomly allocated to be actively helped to find and place pieces; the other group was only encouraged, but was given no assistance. In the post-test trial, the residents who were just encouraged outperformed those who had been helped. Not only did they outperform the other participants, but they rated themselves as more confident in their abilities.

"What has this to do with family practice?" you may ask. A family physician is a mature independent professional who is continually making decisions about other people's lives. Let me raise another question: Are there forces about that may make us dependent, even though this may be happening with the best of intentions?

Let me offer an example. Recently I received an advertisement for *General Practice Video Digest*. It quotes one physician as saying, "I like the experts giving their experience and advice." The editorial board of this publication consists of professors of medicine and surgery from Harvard, Johns Hopkins, and even Toronto. They included a token Canadian, but they didn't even think to include a token family physician.

A recent incident taken from the University of Western Ontario study of headaches illustrates the forces that are at work. Dr. C. prides himself on being a well-informed family doctor. Even though he is very busy, he finds time to read journals regularly, he attends refresher courses, he uses the latest drugs, refers patients to consultants when he is in any doubt, and investigates patients thoroughly so that serious disease is not missed. One patient he enrolled was a 30-year-old woman who presented with a troublesome recurring headache. She was sent for a skull X-ray series and subsequently was seen by a neurologist, who assessed the problem as a muscle-contraction headache. Dr. C. prescribed one of the new non-steroidal anti-inflammatory drugs (NSAIDs) and recommended some techniques for controlling stress.

When I debriefed Doctor C., he explained his thinking. He said that he had suspected a tension headache, but the patient had denied that she had new stresses in her life. The skull films had been recommended in a review article he had read. The referral to a neurologist was primarily to reassure the patient that nothing serious was being missed. He had prescribed the NSAID because a visiting drug-company representative had told him that this new medication was more effective than codeine, but not addictive. Dr. C. had been careful not to start the patient on a narcotic that could be addictive.

Dr. C.'s situation illustrates many of the forces that work on each of us. The literature that we read is predominantly produced by specialists. They do not hesitate to entitle their articles, "What the Family Physician Should Know about TIAs—or Headache or Hypertension". How many of these articles in *Postgraduate Medicine*, *Diagnosis*, or *Modern Medicine* are written by family physicians? The un-

stated message is clear. Who is the boss? Who is the assistant?

The drug detail man arrives bearing information and samples that are beautifully prepared and targeted to the physician's apparent needs. He is only too eager to help, especially if it is with the choice of a drug. One cannot help but notice a resemblance between his easily available assistance and that of the nursing personnel helping the elderly nursing-home resident to get dressed or solve puzzles. The issue in this case is not which drug to prescribe, but how best to help the patient. A drug may not be indicated at all. The specialist is easily accessible for patient referral and for ensuring that serious pathology is not missed. He does not mind in the least being a helper to this busy family physician and may even unconsciously have encouraged the latter's dependence.

And so the review journals, the drug representatives and the helpful specialists are forces fostering learned dependence in the family physician. There are other, less visible influences on the family doctor, as well. There is the view of his role that medical school conditioned him to hold on graduation. Dr. C. had been trained primarily by specialists to detect and treat disease. In a way, he was "harnessed". This narrow concept of his role limits his ability to manage and to heal the illnesses of his patients.

The final force acting on our doctor was a dependence on technology. The physician has become over-reliant on technology to help him/her make decisions. Obviously, my story is several years old. Today the skull X-ray films would be replaced by a CT scan. Fortunately, many physicians shake off the conditioning mentioned above by virtue of their innate independence or their residency training. But many others do not overcome either the conditioning or the other forces. They exist, instead, in a state of learned dependence.

### Does it Matter?

It is always a source of satisfaction to be master of what one does, but has such mastery any real consequences? Dr. C. gave safe, thorough care. He ensured a correct diagnosis, treated the patient's pain with an efficacious drug, and attended to her psychosocial needs by giving anti-stress

instructions. He may have used a few extra resources, but his patient may have expected that, and Canada is well endowed with resources.

But it does matter if the patient isn't helped and the physician is ineffective. Notable family-physician researchers have made the following important points cogently and eloquently:

- No one but ourselves can fully know our needs and our patients' needs.
- No one but ourselves will answer our questions exactly.
- No one has as good an opportunity to study our patients as we do.
- This, of course, does not mean that others haven't a great deal to offer, or that they do not work with similar patients.

### How Does One Go About Shaking Off Learned Dependence?

To claim that there is one remedy for learned dependence, and that that remedy is office-based research, would be to do the readers of this article an injustice equal to that of the well-meaning detail man. In fact, there are many answers. First, the family physician must develop skills of critical appraisal in order to be able to tell whether a new drug is all it is supposed to be. (It never is.) Secondly, it is important to read widely. Eric Cassel, in *The Healer's Art*, opened my eyes to the world of the "sick".<sup>5</sup> He identified their loss of connectedness with the world, their loss of confidence in their own body, and their sense of loss of control. This seems to me to be essential knowledge for one who is to facilitate healing. A third way of breaking free is to listen to the patients. They know more about themselves than any medical text, and they have much to teach us physicians. Finally, office-based research is a powerful means of shaking off learned dependence.

In 1977, Michael Oppenheim of Los Angeles wrote a piece in *Medical Economics* that told how his office experiments spiced up his practice.<sup>6</sup> He was annoyed at the number of patients who wanted to be seen because of colds. Rather than feeling overwhelmed and abused, he undertook a small study. A tally kept over two months showed that of 919 patients, he had seen 200 for colds. Of these,

only 14 needed antibiotics. This finding led him to design a vigorous educational campaign, including office posters and a one-page hand-out that was given as each patient attended. Both patients and doctor were pleased with the new situation that evolved.

In the same article, Dr. Oppenheim wrote about his discontent with the program he was using to help obese patients lose weight. He was taking the standard approach recommended by experts. When he looked at his work closely, however, he saw that only one of 24 patients had benefited. On the basis of that observation, he revised his approach markedly. Dr. Oppenheim was demonstrating curiosity, a willingness to challenge the *status quo*, and the ability to learn from his own experience in the office. He could have swallowed his discontent, gritted his teeth, prescribed the latest recommended drug, and kept on seeing patients whom he was not helping, but his research allowed him to refocus—and to jump over the barrier.

Office-based research reflects what a family physician is about. We are a service profession. Sometimes a physician has the numbers to do the research in his own practice, but often he needs the co-operation of other physicians. Be that as it may, the individual physician learning from his own patients will always be a cornerstone of family-practice research. The challenging questions arise from patients' problems. Often, too, our patients provide us with answers that we see only when our eyes are unblinkered.

A former resident of mine, Dr. Miriam Salamon, had a new mother present with monilial vaginitis. On being told that she had a yeast infection, the patient asked whether she could have caught it from her daughter, who had been diagnosed earlier as having monilia diaper rash. Dr. Salamon gave the standard textbook response that it was the other way about: that transmission was from mother to daughter. But she continued to ponder the question. Eventually she looked at the records of all infants and their mothers in the practice.<sup>7</sup> Of 45 mother-infant pairs, there were nine instances where both the infant and the mother were seen for monilial infections in the same three-month period. In eight of the nine instances,

the mother's infection followed that of the infant by one to two weeks. This observation is not the full answer, but it opens an intriguing new area. It is an ideal situation for exploration by a family physician with an active obstetric practice who cares for babies and their mothers. And it provides an example of a family physician who is exerting independent thought.

The chief problem of doing research in one's own practice is the limited number one sees of any one type of patient. A single practice is good for researching colds, otitis media, common rashes, or patient satisfaction. But many conditions are relatively uncommon, and the physician who wants to evaluate a therapy is limited to trying it on one or two patients in the face of the associated problems of bias and placebo effect. The alternative is to wait until a large randomized trial is undertaken. But just as learned dependence can develop in clinical matters, so, too, it can develop in research. We need to be open to new ideas.

One approach that is ripe for use in family-practice research is an alternative to the randomized trial, which has long been the "gold standard" in assessing the efficacy of therapy. Such a trial often requires large numbers of participants, and even if the necessary numbers are available, it is uncertain whether the therapy will help any specific patient.

A technique of single-subject research used in psychology offers exciting possibilities. Gordon Guyatt and David Sackett of McMaster University have refined it.<sup>8</sup> It requires a situation in which patients have a chronic problem, the effect of the therapy is of limited duration, and outcomes are measurable. Such a combination of circumstances sets the scene for what its originators call an "N-of-1 trial". In such a trial, a single patient undergoes a series of pairs of treatments. Each pair consists of one active and one placebo treatment period. The order is random. Both patient and physician are blinded. The following case illustrates the technique.

A physician wondered how to help his female patient with multiple aches that had been diagnosed as fibrositis. Aspirin and NSAIDs didn't help. He had read that low-dose amitriptyline

might help some patients, but there was no trial evidence. Consequently he did an N-of-1 trial. He had the pharmacy prepare and number two identical sets of capsules, one containing amitriptyline 10 mgm, the other lactose. Each set of capsules was given for a two-week period in two consecutive months. Neither the physician nor the patient knew which set contained the active ingredient. The patient kept a daily diary of her fibrositis symptoms throughout the two-month period. When the code was broken, it was found that the patient had recorded marked relief in both periods during which she was taking the amitriptyline. Both the physician and the patient were convinced that this medication had helped.

This type of trial can be used to study a great many problems: asthma, hypertension, headaches, chronic cough, and others. If the trial is maintained through at least three cycles, the data can be analysed with a paired t-test. Here is an example of a new technique for research. We can always use more tools of this sort.

But to investigate a great many problems that intrigue, trouble, haunt, or stimulate us, we need large groups of patients from many practices. The answer to this situation is that there is strength in numbers. Research networks have met this need in Britain, the Netherlands, Australia, Canada, and the United States. The Ambulatory Sentinel Practice Network (ASPN), for instance, founded by the North American Primary Care Research Group (NAPCRG), has grown steadily and has allowed many physicians to become involved in research. It has also begun to answer some important clinical questions.

To provide examples of successful research networking, I shall describe briefly three recent studies involving numbers of physicians in different ways. Each study helped the family physician to assert his independence and exert control over his environment.

The first example is a study of possible ways to improve the care of hypertensive patients by adopting a new approach. In the 1970s there was serious and frequent criticism of the care of hypertensives: hypertension was being missed or poorly treated. Since family physicians take care of

most hypertensive patients, this constituted direct criticism of the family physician. There were murmurs about setting up hospital-based hypertension clinics. The accusation was made that the family physician had no organized approach to the detection of high blood pressure, prescribed inadequate therapy, ignored problems of patient compliance, and followed up patients haphazardly.

Our department designed strategies to counter each criticism: a screening policy, stepped-care therapy, emphasis on patient compliance and on physician follow-up. A part-time medical assistant was assigned the duty of ensuring that the strategies formulated were carried out.

To find out if this new approach could be put into effect and, more important, if it would make a difference to our patients, we undertook a randomized trial.<sup>9</sup> Our trial required the involvement of 34 practices, half to carry out the interventive strategies and half to serve as controls. We asked all the family physicians within a 48-mile radius of London if they would be interested in participating in a long-term study of a new approach to managing hypertension. An astonishing 50% of the 178 physicians approached said yes! Of these, 34 were chosen and grouped in pairs. One member of each pair was assigned to the experimental interventive group. In all, 32,000 patients were followed for five years.

The results of this research project are summarized in Chart 1. More effective screening of patients took place in the experimental practices. In particular, men under 50 were screened more thoroughly. Although blood pressures were only slightly lowered in

the group given the extra attention, compliance was significantly improved. Our concern that the involvement of a medical assistant would adversely affect patient satisfaction proved to be unfounded. In fact, the opposite was true. Those practices that included a medical assistant were seen as more concerned, more readily available, and as having more appropriate waiting periods. Finally, there was no difference between the two groups in overall incidence of mortality, stroke, or congestive heart failure. The control physicians held their own in managing elevated diastolic blood-pressure, in screening the over-50 age group well, and in preventing morbidity. The main explanation for these results was that those patients with the highest pressures were under care in both types of practice.

The chief conclusion that emerged from this study was that the unassisted family physician can care effectively for patients with high blood pressure. Secondly, minor changes in practice in relation to compliance and waiting times can improve patient care. This was the first study of such duration and scope in Canada. I believe that it helped to convince granting authorities that family physicians can do long-term multi-practice research. Certainly, it convinced me that we can care for hypertensive patients and also do credible research. While the family physicians in the study were important contributors, they did not participate in the design or analysis of the study. They reported that the findings were helpful.

The second study was a more clinical one. The matter it investigated was the natural history of headaches that present in family practice, and what factors predict which headaches will resolve.<sup>10</sup> The study group consisted of 19 family physicians who were involved in the project from the beginning. They helped to choose the topic, contributed to the design, and played a critical role in the data collection. All patients newly presenting with headaches were enrolled in the study and followed for one year. Each physician carried out a standard physical examination and then was asked to offer an assessment of the diagnosis and contributing factors, and to use him/herself as a measuring instrument. Follow-up for the study was done centrally by the research assistant.

The main findings of interest were good data on the prevalence of the different types of headache that present in family practice. Only 22.8% of the headaches had an organic basis. As a result of the one-year follow-up process and tight definitions, we are confident of the categorization. Only one patient, who presented with a new headache of one month's duration and left-leg weakness, was discovered to have a brain tumour.

When we looked at the remaining 77% of headaches, which we called "non-organic", we were struck by the infrequency of classic migraine. Yet migraine sufferers are the group involved in most of the research reported by headache clinics. The physicians participating in our study noted that patients with common migraine and muscle-contraction headache had similar stresses, family histories, and depression scores, as well as similar outcomes. We observed that as the headache pain became more severe, the headache was described as "throbbing", and nausea was more common. It then occurred to us that our terminology was "harnessing" us. We suggested that the term "chronic non-specific headache" would be a more useful concept for the family physician,<sup>11</sup> providing escape from the medical model that a specific stress must cause a tension headache.

What factors predicted resolution of headache within one year? The usual demographic measures of age, sex, and marital status had no effect on outcome, nor did level of anxiety, depression or distress. Drugs and investigation had no effect on long-term outcome. Only three factors, listed in Table 1, made a difference. Organic headaches were 3.2 times more likely than others to resolve. The most powerful predictive factor was the patient's report, early on, that he/she had had an opportunity to discuss fully, with the physician, the headaches and the problems surrounding them.

This factor emphasized the importance of doctor-patient communication. Another factor important to the clinician is distinguishing organic headaches from non-organic. The physician's impression that anxiety was not a contributing factor to the patient's headache was the strongest predictor of the presence of an organic headache. This variable combines the

# **Chart 1** **London Hypertension Study:** **Summary of Results**

## **Experimental Group:**

Greater screening under 50 yrs.  
Greater drug compliance  
Lower systolic blood pressure  
Increased satisfaction

No difference in proportion <100 mmHg diastolic

No difference in morbidity

No difference in mortality

Source: See Reference 9.

physician's experience and knowledge of the patient with the history and physical findings.

Is this approach revolutionary? What has it to do with combatting learned dependence? Learned dependence, as I have shown, can exist in the research sphere, as well as in the clinical sphere. In addition, I have demonstrated that the most potent therapy the physician offered was her/himself, by giving patients the perception that they were being heard. This therapy is more powerful than the NSAIDs or anti-depressants recommended by the friendly detail man or well-meaning consultant. The physicians involved in the research told me that they started to look forward to patients presenting with headache. They felt more confident in their ability to sort out the patients' problems, and they found that they used pharmacotherapy less often.

The third study, too, involved a network of physicians. This study had a three-tiered structure: a group of university-based investigators; a second tier consisting of an intensively involved subgroup of four physicians; and a larger group of 13 physicians who supplied patients. The large question that the study addressed was, "What does the doctor do that makes a difference for patients newly presenting with a symptom?"

The subjects were patients newly presenting with one of seven common symptoms: backache, chest pain, abdominal problems, fatigue, headaches, eye problems, rectal bleeding. These symptoms were chosen because they were common and represented a mix of psychological and organic problems. Patients were followed at four and 12 weeks to determine their state in respect to the symptom(s) and their concern. The second-tier group of four physicians audited the charts blindly. They found that at one month, almost 50% of the symptoms had resolved. Rectal bleeding and eye symptoms were the most likely to settle, and headaches the least likely.

We first looked at the technical aspects of care, the kind that are usually audited. Strikingly, none were associated with resolution of the patients' symptoms. The completeness of the recorded history or examination or investigation was unrelated to outcome. Prescription of drugs had no effect on outcome.

What factors, then, did matter? As Table 2 indicates, a stressed patient was 4.4 times less likely to achieve resolution of the problem. The only physician action that was related to outcome was whether patient and physician agreed on the nature of the problem. Where agreement was reached, resolution was 5.6 times more likely to occur. This finding bears a striking similarity to the headache study in which doctor-patient communication was identified as the critical factor.

Would the friendly drug-detail man ever have told us physicians all this? Would the well-meaning consultant ever address these matters? Do physicians learn about these factors in medical school? Cassel obtained this information from observing his patients; the doctors in our study learned it from their involvement in office-based research.

## Conclusions

Many physicians know that research can be an agent of change. I suggest that it can be a liberating agent, as

well. It can build physician confidence and improve patient care. It can benefit our colleagues as well as ourselves.

In my view, therefore, we physicians involved in research have a responsibility to help our colleagues throw off the yoke of learned dependence. We can do that by developing research networks that involve physicians who, by themselves, might not have the opportunity to engage in research. We can involve others in our research. We can publish research papers that are readable and clinically relevant. Finally, we can identify and oppose the forces that foster our dependence, and we can support those endeavours that tend toward the expansion of our areas of interest and expertise. A journal directed to family physicians should have family-physician representation on its board. Papers written by family physicians should appear in that journal. Solutions may even be found for the learned dependence encouraged by our friendly drug industry and our medical schools.

**Table 1**  
**Factors Associated with Resolution at 12 Months in Patients Newly Presenting with Headache**

	Adjusted relative odds of resolution
Patient reported full discussion of headache with doctor (cf. less than full discussion)	3.4
Organic final diagnosis (cf. non-organic diagnosis)	3.2
Absence of visual problems accompanying headache (cf. presence)	2.2

Source: See Reference 10.

Note: Logistic regression  $p < .05$ .

**Table 2**  
**Physician's Actions and the Resolution of Common Symptoms at Four Weeks**

	Adjusted relative odds of symptom resolving
Patient complete agreement with physician's assessment (cf. partial or non-agreement)	5.6
Patient report stress (cf. no stress)	4.4
Psychosocial factors important (cf. unimportant)	4.6
Symptom present under 2 wks (cf. more than 2 wks)	2.9

Source: See Reference 11.

Note: Logistic regression  $p < .01$ .

**ACTIONS**

LOPID lowers elevated serum lipids primarily by decreasing serum triglycerides with a variable reduction in total serum cholesterol. These decreases occur in the very low density lipoprotein (VLDL) fraction and in the low density lipoprotein (LDL) fraction. In addition, LOPID may increase the high density lipoprotein (HDL) cholesterol fraction. The mechanism of action has not been definitely established. In man, LOPID has been shown to inhibit peripheral lipolysis and to decrease the hepatic extraction of free fatty acids, thus reducing hepatic triglyceride production. LOPID also inhibits synthesis of VLDL carrier apoprotein, leading to a decrease in VLDL.

**INDICATIONS**

LOPID is indicated as an adjunct to diet and other therapeutic measures in management of patients with TYPE IV hyperlipidemia who are at high risk of sequelae and complications from their hyperlipidemia.

Initial therapy for hyperlipidemia should include a specific diet, weight reduction, and an exercise program and for patients with diabetes mellitus, a good diabetic control.

**CONTRAINDICATIONS**

1. Hepatic or renal dysfunction, including primary biliary cirrhosis.
2. Pre-existing gallbladder disease. (See Precautions)
3. Hypersensitivity to gemfibrozil.
4. The drug should not be used in pregnant and in lactating patients.

**WARNINGS**

1. Concomitant Anticoagulants — Caution should be exercised when anticoagulants are given in conjunction with LOPID. The dosage of the anticoagulant should be reduced to maintain the prothrombin time at the desired level to prevent bleeding complications.
2. Long-term studies with gemfibrozil have been conducted in rats and mice at one and ten times the human dose. The incidence of benign liver nodules and liver carcinomas was significantly increased in high dose male rats. The incidence of liver carcinomas was increased also in low dose males, but the increase was not statistically significant ( $P > 0.05$ ). There were no statistically significant differences from controls in the incidence of liver tumors in female rats and in male and female mice. Liver and testicular cell tumors were increased in male rats.
3. Cholelithiasis — LOPID may increase cholesterol excretion into the bile leading to cholelithiasis. If cholelithiasis is suspected, gallbladder studies are indicated. LOPID therapy should be discontinued if gallstones are found.
4. Since a reduction of mortality from coronary artery disease has not been demonstrated, LOPID should be administered only in those patients described in the Indications section. If a significant serum lipid response is not obtained in 3 months, LOPID should be discontinued.
5. Safety and efficacy in children have not been established.
6. Strict birth control procedures must be exercised by women of childbearing potential. If pregnancy occurs despite birth control procedures, LOPID should be discontinued.
7. Women who are planning pregnancy should discontinue LOPID several months prior to conception.

**PRECAUTIONS**

1. **Initial Therapy** — Before instituting LOPID therapy, attempts should be made to control serum lipids with appropriate diet, exercise, weight loss in obese patients, and control of diabetes mellitus.
2. **Long-term Therapy** — Because long-term administration of LOPID is recommended, pretreatment chemistry studies should be performed to ensure that the patient has elevated serum lipid or low HDL cholesterol levels. Periodic determinations of serum lipids should be obtained during LOPID administration.
3. **Impairment of Fertility** — Administration of approximately three and ten times the human dose to male rats for 10 weeks resulted in a dose-related decrease of fertility. Subsequent studies demonstrated that this effect was reversed after a drug-free period of about 8 weeks, and it was not transmitted to their offspring.
4. **Hemoglobin Changes** — A mild hemoglobin or hematocrit decrease has been observed in occasional patients following initiation of LOPID therapy. The levels then stabilize during long-term administration. Therefore a blood count is recommended every two months during the first 12 months of LOPID administration.
5. **Liver Function** — Abnormal liver function tests have been observed occasionally during LOPID administration, including elevations of SGOT, SGPT, LDH, and alkaline phosphatase. These are usually reversible when LOPID is discontinued. Therefore periodic liver function studies are recommended and LOPID therapy should be terminated if abnormalities persist.
6. **In patients with past history of jaundice or hepatic disorder, LOPID should be used with caution.**
7. **Cardiac arrhythmias** — Although no clinically significant abnormalities occurred that could be attributed to LOPID, the possibility exists that such abnormalities may occur.

**ADVERSE REACTIONS**

Gemfibrozil has been carefully evaluated in over 3,000 patients having received the drug in monitored clinical studies. Symptoms reported during the controlled phase in studies of 805 subjects were considered for safety. The symptoms listed below are those which occurred in at least 5 patients and all skin reactions whatever their incidence. The principal symptoms for which incidence was greater with gemfibrozil than with placebo involved the gastrointestinal system. Nausea and vomiting, abdominal and epigastric pain occurred more often in the gemfibrozil group than in the placebo group. However, the incidence was low: nausea, 4.3% with gemfibrozil versus 3.8% with placebo; vomiting, 2.3% versus 0.8%; abdominal pain, 6.4% versus 4.2%; and, epigastric pain, 3.4% versus 1.7%.

**SYMPTOMS AND TREATMENT OF OVERDOSAGE**

While there has been no reported case of overdosage, symptomatic supportive measures should be taken should it occur.

**DOSAGE AND ADMINISTRATION**

The recommended dose for adults is 1200 mg administered in two divided doses 30 minutes before the morning and evening meal. The maximum recommended daily dose is 1500 mg.

**AVAILABILITY**

The colour of LOPID capsules is maroon and white. Each capsule contains 300 mg gemfibrozil and is available in bottles of 100.

In summary, there are subtle forces that foster our dependence, both clinically and in research. Innovative office-based research is an important way of jumping over the barrier. We can help others, too, to become aware of their dependence, and we can help them to jump over the barrier, in their turn. Opportunities exist. I hope that we will find the energy and interest to grasp them. ●

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